REMARKS

Applicants previously filed a Notice of Appeal on September 4, 2008. Accordingly, this paper is submitted in connection with a Request for Continued Examination that is being filed in lieu of an Appeal Brief in the above-identified application.

Upon entry of the amendments made herein, claims 1, 37-47, 54, 57, 59-60, and 62-65 are pending in this application. By this amendment, Applicants have amended claims 1, 59, 60, 62 and 64, canceled claims 58 and 61 without prejudice or disclaimer, and added new claim 65. Claims 2-36, 48-53, 55 and 56 were previously canceled.

Claim 1 has been amended to further define the claimed invention. Support for these amendments can be found in the specification and in expressly incorporated references described therein. Specifically, support for the limitation "DTMR associated with splicing of nuclear RNA" can be found, for example, on page 3, lines 32-34 of the specification as filed. Furthermore, support for "spinal muscular atrophy" can be found, for example, on pages 240-241 of Philips *et al.* (2000), Cell. Mol. Life Sci., 57:235-249 and on page 21 of Stoss *et al.*, (2000), Gene Ther. Mol. Biol. 5:9-30 (courtesy copies enclosed), each of which is expressly incorporated by reference in the instant specification on page 9, lines 14-17 and lines 28-29 and page 102, lines 14-16 of the specification.

Claims 59, 60, 62 and 64 have been amended to correct claim dependencies and to correct various typographical errors.

New claim 65 has been added to further define the invention. Support for claim 65 can be found, *e.g.*, on page 17, row 1, column 1 of the specification and in the claims as originally filed.

Accordingly, no new matter has been added.

Double Patenting

Claims 1 and 37-47 have been rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims in each of U.S. Patent Nos. 6,500,812; 6,624,168; 6,642,270; 6,683,068; 6,818,634; 6,818,635; 6,846,939; 6,849,615; 7,045,507; and 7,094,806. According to the Examiner, these U.S. patents teach methods of treating a subject with a bacterial infection, fungal infection, or a tetracycline responsive state

such as cancer. Thus, the Examiner concludes that the claims in each cited patent are more narrowly drawn than the corresponding genus claims recited in the instant application. (*See* Office Action at p. 6). Applicants traverse these rejections.

The currently amended claims are drawn to a method for treating a subject for a DTMR (disease treatable by the modulation of RNA) associated with splicing of nuclear RNA, wherein the DTMR is spinal muscular atrophy (SMA). Each of the patents cited above fail to teach or suggest the use of tetracycline compounds for the treatment of disorders associated with the splicing of nuclear RNA, such as spinal muscular atrophy. Thus, in view of the disclosures of the patents cited above, one of ordinary skill in the art would not have reasonably expected that tetracycline compounds would be effective at treating spinal muscular atrophy associated with splicing of nuclear RNA. As such, Applicants submit that the claimed treatment methods would not be obvious in view of these patents and request reconsideration and withdrawal of these double patenting rejections.

Claims 1 and 36-47 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of copending Application Nos. 10/692,563; 10/752,378 (now U.S. Patent No. 7,323,492); 10/786,881; and 10/943,571. According to the Examiner, these copending applications teach methods of treating malaria, bacterial infections, fungal infections, and tetracycline responsive states. Because the definition of a DTMR encompasses the specific diseases and disorders disclosed in these patent applications, the Examiner concludes that the claimed method of treating a DTMR would include a method of treating a bacterial infection, a fungal infection, or a tetracycline responsive state using an effective amount of tetracyclines. (*See* Office Action at p. 9). Applicants traverse these rejections.

As an initial matter, Applicants note that claim 36 has been canceled. Thus, this rejection is moot as it applies to this claim. For the remaining claims subject to this rejection, the currently amended claims are drawn to a method for treating a subject for a DTMR associated with splicing of nuclear RNA, wherein the DTMR is spinal muscular atrophy (SMA). The applications cited by the Examiner above fail to teach or suggest the use of tetracycline compounds for the treatment of disorders associated with the splicing of nuclear RNA, such as spinal muscular atrophy. Thus, in view of the disclosures of the cited

applications, one of ordinary skill in the art would not have expected that tetracycline compounds would be effective at treating spinal muscular atrophy associated with the splicing of nuclear RNA. Accordingly, Applicants submit that the claimed methods would not be obvious in view of these applications and request reconsideration and withdrawal of these double patenting rejections.

Enablement

Claims 1, 36-47, 54 and 57-64 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. According to the Examiner, "the skilled artisan would have to conduct undue and excessive experimentation in order to practice the claimed invention." (*See* Office Action at p. 20). Specifically, the Examiner notes that the invention involves a method of treating *any* DTMR associated with splicing by administering *any* tetracycline derivative to *any* subject. (*See* Office Action at p. 12). Furthermore, according to the Examiner, there is no disclosure in the specification regarding how the modulation of RNA occurs, how to evaluate which tetracycline compounds have effects on different diseases, how a skilled artisan would decide between two different tetracycline derivatives, and the particular genes that are modulated in Example 3. (*See* Office Action at pp. 11-20). Applicants traverse the rejection.

Detailed procedures for making and using the invention may not be necessary to meet the standard for enablement if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention. (*See* MPEP § 2164). The standard for determining whether the specification meets the enablement requirement is determining whether any experimentation needed to practice the invention is undue or unreasonable. (*See* Mineral Separation v. Hyde, 242 U.S. 261, 270 (1916); In re Wands, 858 F.2d. 731, 737 (Fed. Cir. 1988)). The fact that experimentation may be complex does not necessarily make it undue, if the art typically or routinely engages in such experimentation. (*See* In re Wands, 858 F.2d. at 737 (Fed. Cir. 1988)). Moreover, as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. § 112 is satisfied. (*See* In re Fisher, 427 F.2d. at 839 (CCPA 1970)).

As an initial matter, Applicants note that claim 36 has been canceled. Thus, this rejection is moot as it applies to this claim. The remaining claims subject to this rejection are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA, wherein the DTMR is spinal muscular atrophy (SMA). As such, the pending claims describe the treatment of a single DTMR, namely SMA, that is associated with the splicing of nuclear RNA.

The instant specification describes several ways in which the modulation of RNA can occur. (*See e.g.,* page 3, line 25 through page 7 line 28 of the specification as originally filed.). Moreover, Applicants submit that the evaluation of the effect of various tetracycline compounds on an SMA disease state is within the routine knowledge of a skilled artisan. For example, the modulation of RNA is described in the specification by direct or indirect binding (*see e.g.*, page 7, line 29 through page 8, line 3), by altering RNA transcription (*see e.g.,* page 4, lines 22-33), by altering RNA translation (*see e.g.*, page 5, lines 4-14), by altering the half-life of RNA (*see e.g.*, page 5, line 33 through page 6, line 5), by altering the translocation of RNA (*see e.g.*, page 6, lines 15-24), and/or by altering the interactions of proteins with RNA (*see e.g.*, page 7, line 22 through page 8, line 22). Methods for the detection of RNA modulation are also described in the specification. (*See e.g.*, page 8, lines 23-26).

Furthermore, the gene modulated in the claimed treatment of SMA is the survival of motor neuron gene (SMN), as described in the incorporated references Philips *et al.* (2000), Cell. Mol. Life Sci., 57:235-249 and Stoss *et al.*, (2000), Gene Ther. Mol. Biol. 5:9-30 (courtesy copies attached).

Likewise, Applicants have also described methods for identifying tetracycline compounds for treating a specific DTMR, such as SMA, as presently claimed. (*See e.g.*, page 11, lines 8-19 of the specification as originally filed). Such methods include measuring the ability of a tetracycline compound to modulate RNA using any of the methods described above and comparing experimental results for a number of tetracycline compounds to identify those having superior properties for the treatment of SMA. A skilled artisan would be able to routinely screen multiple tetracycline compounds to determine the best candidate(s) for the treatment of SMA.

In view of the above, Applicants submit that the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim. Likewise, the incorporated references, Philips *et al.* and Stoss *et al.*, describe the specific DTMR recited in the instant claims as well as the particular gene involved in the disorder to be treated. As a result, one of ordinary skill in the art with the specification in hand would be able to practice the claimed invention without undue experimentation.

Accordingly, Applicants submit that the enablement rejection has been overcome and should be withdrawn.

Written Description

Claims 1, 36-47, 54 and 57-64 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner notes that DTMRs associated with splicing are not specifically defined and that the claims read on a genus of methods of any *in vivo* or *in vitro* treatment of any DTMR associated with splicing using any tetracycline compound. (*See* Office Action at pp. 23-24). Moreover, the Examiner also contends that Applicants have not provided any data providing evidence for the *in vivo* treatment of any DTMR associated with splicing using any of the tetracycline compounds described and that Applicants do not provide explicit instructions on how to differentiate between the advantages of using one tetracycline compound over another. (*See* Office Action at p. 24). Based on this, the Examiner contends that the skilled artisan would conclude that Applicants were not in possession of the claimed invention. (*See* Office Action at p. 25). Applicants traverse the rejection.

As an initial matter, Applicants note that claim 36 has been canceled. Thus, this rejection is moot as it applies to this claim. The remaining claims subject to this rejection are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA, wherein the DTMR is spinal muscular atrophy. As such, the pending claims describe the treatment of a single DTMR, namely SMA, that is associated with the splicing of nuclear RNA.

As discussed above, the evaluation of the effect of various tetracycline compounds on an SMA disease state is within the routine knowledge of a skilled artisan. For example, the modulation of RNA is described in the specification by direct or indirect binding (*see e.g.*, page 7, line 29 through page 8, line 3), by altering RNA transcription (*see e.g.*, page 4, lines 22-33), by altering RNA translation (*see e.g.*, page 5, lines 4-14), by altering the half-life of RNA (*see e.g.*, page 5, line 33 through page 6, line 5), by altering the translocation of RNA (*see e.g.*, page 6, lines 15-24), and/or by altering the interactions of proteins with RNA (*see e.g.*, page 7, line 22 through page 8, line 22). Methods for the detection of RNA modulation are also described in the specification. (*See e.g.*, page 8, lines 23-26).

Moreover, the gene that is modulated in these treatment methods is the survival of motor neuron gene (SMN), as described in the incorporated references Philips *et al.* (2000), Cell. Mol. Life Sci., 57:235-249 and Stoss *et al.*, (2000), Gene Ther. Mol. Biol. 5:9-30 (courtesy copies enclosed).

Applicants have also described methods for identifying tetracycline compounds for treating a specific DTMR, such as SMA. (*See e.g.*, page 11, lines 8-19 of the specification as originally filed). These methods include measuring the ability of a tetracycline compound to modulate RNA and comparing the experimental results for a number of tetracycline compounds to identify compounds having superior properties for the treatment of SMA. A skilled artisan would be able to routinely screen multiple tetracycline compounds and determine the best candidate(s) for the treatment of SMA.

Thus, contrary to the Examiner's contention, Applicants submit that the specification and the incorporated references describe the claimed invention in sufficient detail such that a skilled artisan would conclude that Applicants had possession of the claimed invention at the time the application was filed. As such, this rejection has been overcome and should be withdrawn.

35 U.S.C. 102

Claims 1, 37-38, 58 and 60-62 have been rejected under 35 U.S.C. §102(b) as being anticipated by Yrjanheikki *et al.* (PNAS, 1998 (95) 15769-15774) ("Yrjanheikki').

According to the Examiner, Yrjanheikki teaches the administration of doxycycline, minocycline and tetracycline for the treatment of ischemia. (*See* Office Action at pp. 29-30). Because the Examiner contends that cerebral ischemia reads on a DTMR associated with splicing, the Examiner concludes that Yrjanheikki teaches the claimed invention. Applicants traverse the rejection.

The currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Yrjanheikki does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending claims are not anticipated by Yrjanheikki. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Nelson *et al.* (US Patent No. 6,500,812) ("Nelson '812").

According to the Examiner, Nelson '812 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing, as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 31-32). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Nelson '812 does not expressly or inherently teach the treatment of SMA or modulation of the splicing of nuclear RNA. Therefore, the currently pending claims are not anticipated by Nelson '812. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Nelson *et al.* (US Patent No. 6,624,168) ("Nelson '168").

According to the Examiner, Nelson '168 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing,

as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 32-33). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Nelson '168 does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending claims are not anticipated by Nelson '168. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Nelson *et al.* (US Patent No. 6,642,270) ("Nelson '270).

According to the Examiner, Nelson '270 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing, as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 34-35). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Nelson '270 does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending claims are not anticipated by Nelson '270. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Nelson *et al.* (US Patent No. 6,683,068) ("Nelson '068).

According to the Examiner, Nelson '068 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing, as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 35-36). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Nelson '068 does not teach the treatment of SMA or the modulation of

splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending claims are not anticipated by Nelson '068. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Nelson *et al.* (US Patent No. 6,818,634) ("Nelson '634").

According to the Examiner, Nelson '634 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing, as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 37-38). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). As Nelson '634 does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently, the currently pending claims are not anticipated by Nelson '634. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Nelson *et al.* (US Patent No. 6,818,635) ("Nelson '635").

According to the Examiner, Nelson '635 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing, as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 38-39). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Nelson '635 does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending claims are not anticipated by Nelson '635. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Nelson *et al.* (US Patent No. 6,846,939) ("Nelson '939).

According to the Examiner, Nelson '939 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing, as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 40-41). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Nelson '939 does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending claims are not anticipated by Nelson '939. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Nelson *et al.* (US Patent No. 6,849,615) ("Nelson '615").

According to the Examiner, Nelson '615 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing, as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 41-42). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). As Nelson '615 does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently, the currently pending claims are not anticipated by Nelson '615. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Draper *et al.* (US Patent No. 7,045,507) ("Draper '507").

According to the Examiner, Draper '507 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing,

as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 43-44). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Draper '507 does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending claims are not anticipated by Draper '507. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Nelson *et al.* (US Patent No. 7,094,806) ("Nelson '806").

According to the Examiner, Nelson '806 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing, as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 44-45). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Nelson '806 does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending claims are not anticipated by Nelson '806. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Draper *et al.* (US Publication No. 20040242548) ("Draper '548").

According to the Examiner, Draper '548 teaches a method of treating a tetracycline responsive state, such as malaria, which inherently reads on a DTMR associated with splicing. (*See* Office Action at pp. 46-47). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Draper '548 does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending

claims are not anticipated by Draper '548. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Huss *et al.* (US Publication No. 20040266740, now US Patent No. 7,323,492) ("Huss").

According to the Examiner, Huss teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing, as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 47-48). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Huss does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending claims are not anticipated by Huss. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Nelson *et al.* (US Publication No. 20050026876) ("Nelson '876").

According to the Examiner, Nelson '876 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing, as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 49-50). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Nelson '876 does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending claims are not anticipated by Nelson '876. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Finally, claims 1, 37-47 and 62 have been rejected under 35 U.S.C. §102(e) as being anticipated by Draper *et al.* (US Publication No. 20050070510) ("Draper '510").

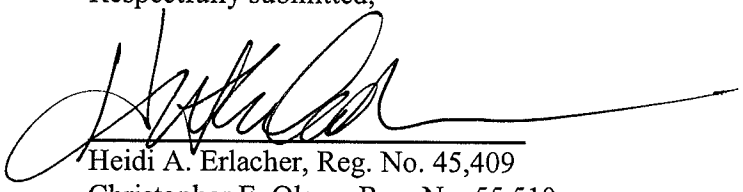
According to the Examiner, Draper '510 teaches a method of treating a tetracycline responsive state, such as cancer, which inherently reads on a DTMR associated with splicing, as the instant specification teaches that cancers are a DTMR associated with splicing. (*See* Office Action at pp. 50-51). Applicants traverse the rejection.

As noted, the currently pending claims are drawn to methods for treating a subject for a DTMR associated with splicing of nuclear RNA wherein the DTMR is spinal muscular atrophy (SMA). Draper '510 does not teach the treatment of SMA or the modulation of splicing of nuclear RNA, either expressly or inherently. Therefore, the currently pending claims are not anticipated by Draper '510. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

CONCLUSION

Applicants respectfully submit that this application is in condition for allowance. If there are any questions regarding this amendment and/or these remarks, the Examiner is respectfully requested to telephone the Applicants' attorney undersigned.

Respectfully submitted,



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